

## ADRENALIN MYDRIASIS IN DEMENTIA PRECOX.

AFTER reading the recent contribution of J. H. Schultz (*Monat. f. Psy. u. Neur.*, 1915, Vol. 37, pages 205-227) and the little treatise of Richard Cords, of Bonn (*Die Adrenalinmydriasis und ihre Diagnostische Bedeutung*, 1911), we find ourselves possessed of a new diagnostic symptom in cases of dementia precox or cases where the diagnosis lies between this condition with its melancholy prognosis, and more hopeful diseases. In the great bulk of healthy persons and sick people as they come to the clinic, there is no reaction of the pupil to 1:1000 adrenalin solution into the conjunctival sac. Even if this is repeated for three or four times, at intervals of two or three minutes, there is no mydriasis at the end of ten minutes, a half hour, an hour, or any longer time.

In cases of indubitable dementia precox, however, mydriasis comes on at the end of ten minutes and it persists for half an hour, or even longer. Out of sixty cases of dementia precox examined by Schultz, forty-six gave a positive reaction, twenty-eight were very strong, seven showed mild mydriasis, while eleven exhibited the paradox of a pupillary contraction.

In order to understand at all the significance of this test upon the pathology of dementia precox, it is necessary for us to consider briefly and incompletely the history of ocular adrenalin reactions.

In 1898, Max Radziejewski (*Berl. k. Woch.*, 1898, Vol. 35, page 572) reported the instillation of a 10 per cent. extract of the adrenal gland into the conjunctival sac of five hundred patients. He noticed no dilatation of the pupil and no changes in accommoda-

tion. About the same time, however, Lewandowsky demonstrated on cats some very valuable facts (Z. f. Phys., 1898, Vol. 12, page 599) relative to the action of adrenal extract in the cat's eye. He found that the intravenous injection of adrenal extract produced the same effect as the stimulation of the cervical sympathetic, namely, mydriasis, retraction of the nictating membrane, slight protrusion of the globe and slight opening of the lids. With large doses of the extract the mydriasis was maximal, and eserine did not completely obliterate it. This mydriasis appeared in a few seconds after the injection and continued only a few minutes. The mydriasis was synchronous with the pressor symptoms, but they showed themselves a little later and passed away more tardily. In rabbits the ocular reactions were less obvious and weaker. When Lewandowsky cut the sympathetic and extirpated the superior sympathetic ganglion, the effect of the injection remained the same. Even a long time after extirpation the reaction remained unchanged. Though electric stimulation of the sympathetic produced the same effect as the intravenous injection of adrenal extract, the effect of the latter was not affected or changed by the extirpation of the superior sympathetic ganglion. Boruttau (Arch. f. d. ges. Phys., 1899, Vol. 78, page 97) confirmed these observations and further called attention to the blanching of the conjunctival sac on the instillation of adrenal extract.

Then came the pure adrenalin of Takamine (Ther. Gaz. 1901, Vol. 25, pages 221 to 224), to which Aldrich (Am. Jour. of Phys., 1901, Vol. 5, page 457, and Vol. 7, pages 359-368) gave the correct empirical formula, and afterward all the experimental work of Stolz (Ber. d. chem. Gesel., 1904, Vol. 14, page 4149) and his better known followers in the synthesis of adrenalin and the reaction and potency studies of the various modified conditions of this base, both from

a chemical and from an optical standpoint, made all research much more reliable and the conditions of research more explicit.

The Meltzers have studied the action of adrenalin on the pupil under almost every conceivable experimental condition. They demonstrated its action on the isolated frog's eye and its use as a test for the efficiency or potency of adrenalin products and solutions. They found the mydriatic action of adrenalin greater after complete extirpation of the superior cervical ganglion than when the sub-ganglion sympathetic was simply cut. These experiments were made on rabbits, and after section of the sympathetic a subcutaneous injection of adrenalin in rare instances produced a slight and scarcely recognizable mydriasis, which quickly disappeared, but after the extirpation of the ganglion a dose of 0.001 gram produced a dilatation of the pupil in ten to fifteen seconds that lasted an hour or two. After ganglion extirpation the instillation of adrenalin solution into the conjunctival sac (four or five times a few minutes apart) produced the maximum mydriasis in two or three minutes, and this was not overcome by eserine and it appeared even if an eserine myosis had been previously established. These effects were first produced twenty-four hours after the excision of the ganglion and they remained even thirty months later, though somewhat modified and retarded.

During an interval, beginning twenty-four hours after extirpation of the pancreas and lasting until sixty-five hours after the operation, Löwi (Wien. k. Woch., 1907, Vol. 20, page 782, and Arch. f. Exp. Path. u. Phar., 1908, Vol. 59, page 83) found that the subconjunctival instillation of 1:1000 adrenalin solution which produced no reaction on normal cats and dogs, and little effect even in guinea pigs and rabbits, produced in the animals from whom the pancreas had been removed a mydriasis beginning in

twenty to sixty minutes and lasting six hours. The instillation of eserine still produced prompt myosis.

Zak (Verhandl. d. 25 Kong. f. inn. Med., 1908, Vol. 25, page 392, and Arch. f. d. ges. Phys., 1910, Vol. 132, page 147), by simply scratching or scarifying the duodenum and its mesentery and the stomach produced adrenal pupillary mydriasis at once after the operation, and he repeated the same condition in man in paritonitis and in one case of meningitis.

This mydriasis seems to be associated with experimental glycemia for Beidel and Offer (Wien. k. Woch., 1907, Vol. 20, page 1530), by ligating the thoracic duct and by producing a chylous fistula, produced a glycosuria and a coincident adrenalin susceptibility and mydriasis.

In trying to measure the significance of the mydriatic phenomena in dementia precox we naturally look not only to anatomy and physiology, but also to pathology and experimental pathology. In what other conditions are similar phenomena observed?

Bittdorf (Zeit. f. inner. Med., 1909, Vol. 30, page 33) observed an adrenalin mydriasis in a case of facial paralysis, and Cords (his monograph, page 18) records a case of gunshot wound of the temple, with transitory paralysis of the first branch of the fifth and of the abducens and a complete paralysis of the trochlear and the sympathetic in which he had a mydriasis of the right eye on adrenalin instillation.

Zak (*l. c.* No. 1) reported a carcinoma of the soft palate with metastasis in the lymph glands of the left side of the neck and paralysis of the sympathetic. There was myosis of the left pupil, but the instillation of adrenalin solution 1:1000 in both eyes resulted in a maximum mydriasis in the left but no reaction in the right eye.

Gautrelet (Arch. d'ophth. 1909, Vol. 29, page 222) reported a stab wound of the left side, one centimeter below the lower jaw, with paralysis of one vocal

cord, the vagus and the sympathetic. There was retraction of the eyeball and myosis. Four months after the injury, both eyes were instilled with three drops of adrenalin solution 1:1000 and there was a slight mydriasis of the left pupil, but two more drops produced, after fifteen minutes, a remarkable mydriasis of the left pupil which continued for half an hour. The identical treatment of the right eye produced no effect.

Cords (*l. c.*, page 53) recounts a parallel experience from the Ophthalmic Clinic of Leipzig. A woman, eighty-one years old, had been operated years before for a carcinoma of the right cheek and now had a carcinoma of the right orbit. There were several masses on the under border of the bony orbit that rendered the globe practically immovable. There was complete paralysis of the first and second branches of the fifth nerve and ptosis. Vision was sufficient to recognize figures at two yards. The cornea was covered by the upper lid and was normal. There was no vasomotor disturbance. The right pupil reacted a little slower to light than the left. The left pupil dilated with a 3 per cent. cocaine solution. The right pupil remained unchanged. But after the instillation of both eyes with a 1:1000 solution of adrenalin the right pupil at the end of a half hour was dilated (6. cmm.) in a bright light while the left was unchanged. It seems likely that the sympathetic was involved by the tumor mass in the orbit itself, perhaps the ciliary ganglion was destroyed.

Cords reports also two other cases of injury at the base of the skull, one from a gun-shot wound and the other from a compound fracture of the base with the destruction of the sympathetic and the disappearance of the adrenal pupillary reaction.

Shima and Zák have observed the adrenalin mydriasis in destructive disease of the brain and cord. Shima (*Arch. f. d. ges. Phys.*, 1909, Vol. 126, p. 269,

and Vol. 127, page 99) observed mydriasis after lesions of the frontal lobe and also of the medulla. Zak (Arch. f. d. ges. Phys., 1910, Vol. 132 page 147) observed adrenalin mydriasis in two cases of tuberculous meningitis, in which the mydriasis was maximal, and one case of hydrocephalus, in one case of diffuse sclerosis of the brain, in one case of miliary tuberculosis, and in one case of post-encephalitic residue in the brain with epilepsy. Zak discusses the relation of the mydriasis to glycosuria.

Zak's experiments on animals and also in men would indicate that a scarifying of the intestine, especially the duodenum, resulted in a susceptibility to an adrenalin mydriasis. He injected two dogs with a 10 per cent. solution of caustic soda into the duodenum and brought about a transitory glycosuria and adrenalin mydriasis. Both symptoms had disappeared by the end of forty-eight hours. Vigorous cauterization of the rectum and large intestine produced no such result. In rabbits, the maximal adrenalin mydriasis appeared in three-quarters of an hour after the cauterization of the stomach.

In the clinical literature only a few cases of a similar nature have been reported by Zak and Bittdorf. These included pelvic peritonitis from abortion, intestinal obstruction, appendicitis, obstruction of the common duct, carcinoma of the stomach and even ulcer of the stomach. The myosis from morphine did not prevent the appearance of the adrenalin mydriasis.

Besides a few cases of glycosuria and diabetes mellitus a number of instances of disturbances of the glands of internal secretion show this anomaly. Löwi, however, did not find this reaction in a case of diabetes with acromegaly. Epinger,<sup>1</sup> Falta and Rudinger, demonstrated this symptom in only four of twenty cases of exophthalmic goitre.

The pupillary reaction in dementia precox is sim-